DEPARTMENT OF THE NAVY
BUREAU OF MEDICINE AND SURGERY
2300 E STREET NW
WASHINGTON DC 20372-5300

IN REPLY REFER TO
BUMEDINST 6000.12A
BUMED-05B1
14 Mar 2000

BUMED INSTRUCTION 6000.12A

From: Chief, Bureau of Medicine and Surgery
To: Ships and Stations Having Medical Department Personnel

Subj: CLINICAL INVESTIGATION PROGRAM (CIP)

Ref: (a) DoD Directive 6000.8 of 3 Nov 99 (NOTAL)
(b) BUMEDINST 5721.3
(c) SECNAVINST 3900.39B
(d) 32 CFR Part 219 (NOTAL)
(e) SECNAVINST 3900.38B
(f) BUMEDINST 6710.69

Encl: (1) What Is and Is Not A Clinical Investigation
(2) CIP Acronyms

1. Purpose. To establish policy, specify authority, and assign responsibility for the Navy medical CIP. Implementing guidance will be issued by the Naval School of Health Sciences (NSHS), Bethesda, MD.

2. Cancellation. BUMEDINST 6000.12.

3. Definition. Clinical investigation is any research program, project, task, test, experiment, record review, evaluation, or similar undertaking that uses data collected from DoD health care beneficiaries, laboratory animals, or *in vitro* to study the maintenance of health or the prevention, alleviation or cure of disease, and whose primary purpose is designed with the intent to develop or contribute to generalized knowledge. Enclosure (1) provides additional guidance.

4. Acronyms. Enclosure (2) provides a complete list of acronyms used in this instruction.

5. Scope. Under reference (a), this instruction applies to all medical and dental activities. Research and development to support the operational mission of the Navy or Marine Corps, using research, development, test, and evaluation funds are exempted from this instruction, except when carried out in a medical treatment facility (MTF) involving beneficiaries of the Naval Medical Department.

6. Objectives. The CIP is an essential component of graduate medical education and state-of-the-art medical care in the Navy. The following are the established CIP objectives:

a. Promote accreditation of graduate medical education programs; provide an academic environment with high professional standing and parity with comparable civilian institutions.

b. Generate an atmosphere of scientific inquiry essential to accommodate the dynamics of patient care, graduate medical education, and other facets of the health sciences.

c. Improve the quality of care for Navy beneficiaries.

7. Policy

a. The Commanding Officer (CO), NSHS Bethesda is the program manager for the CIP and maintains final approval and suspension authority over all protocols under the Program. The CO, NSHS Bethesda may delegate authority annually to commanders of naval MTFs with clinical investigation departments (CID) for the approval of protocols, per their operating guidance, with the exceptions of studies using dogs, cats, marine mammals, nonhuman primates, and retrovirology research.

b. Animal use protocols involving dogs, cats, marine mammals, and nonhuman primates will be reviewed and approved by the Special Assistant for Veterinary Medicine (MED-02E). Other animal research (i.e., mice, gerbil, pig, etc.) may be approved locally and should be forwarded to MED-02E and to the CO, NSHS Bethesda for information.

c. Retrovirology (HIV-1, HIV-2, or HTLV-1) protocols will be reviewed and must be favorably endorsed by the Bureau of Medicine and Surgery (BUMED) HIV Program Branch (MED-02H) before implementation.

d. Department of Defense personnel are prohibited from accepting compensation in addition to their regular salaries for conducting clinical investigation studies.

e. Only persons entitled to care in MTFs are eligible to participate as human subjects.

f. Data collected as a result of an approved CIP protocol is the property of the Department of the Navy and must be cleared per reference (b). To be released, the data must be for the benefit of medical science and not for the profit of private parties. When released for publication, interpretative findings and opinions must be identified as those of the author, and not those of the Navy.

g. CIP investigators may not maintain custody of funds or other resources obtained for support of the protocol. These resources must remain under the control of the comptroller at the medical activity facilitating the research, or a third party specified under an approved memorandum of understanding or other authorized, written support agreement.

h. Clinical investigation projects are subject to military contingency requirements and may not compete with available commercial facilities in providing special services to agencies outside the Federal Government.

i. CIP investigators who plan to collaborate with investigators from other institutions must provide evidence of approval by the other institute's laboratory animal care and use committee, committee for the protection of human subjects, or institutional review board, when applicable. A copy of the appropriately executed resource sharing agreement with the comptroller, staff judge advocate, and commander's approval, is required.

j. NSHS Bethesda will review all requests to sponsor an investigational agent before submission to the Food and Drug Administration. Since Navy investigators may be transient, enrolled subjects must be guaranteed follow-up treatment. A request for an individual investigator to sponsor an investigational agent will not be approved. All requests for sponsorship must be from the commander of the MTF where the study will be performed.

k. All biomedical research must be approved by the CIP, the Director, Research and Development (MED-26), or other organizations authorized by the Navy. Approved research must be conducted in compliance with Navy and Federal policy, and comply with ethical guidelines (i.e., Belmont Report, Nuremberg Code, World Medical Association Declaration of Helsinki, etc.).

8. Responsibilities

a. Chief, BUMED

(1) Establishes policy and maintains total program oversight for CIP.

(2) May delegate appropriate approval and implementing authority to the CO, NSHS Bethesda.

(3) Performs periodic inspections of facilities, identifies areas of noncompliance, recommends appropriate corrective actions, and recommends policy changes, as required.

b. CO, NSHS Bethesda

(1) Publishes guidance detailing the specifics of the CIP; provides standard formats, outlines for CIP procedures, requirements, protocol submissions, and documentation.

(2) May delegate authority for protocol approval to the commander of naval MTFs with CIDs, as specified in this instruction.

(3) Takes final action on recommendations of the Special Assistant for Veterinary Medicine (MED-02E), and the HIV Program Branch (MED-02H), when authorized by BUMED.

(4) Advises BUMED on all budget and implementation issues pertaining to the CIP and administers centrally funded aspects of the program including CIP investigator travel.

(5) Maintains the official central record system for the CIP.

(6) Prepares annual CIP summary reports for the Chief, BUMED and the Deputy Chief, Office of the Assistant Secretary of Defense (Health Affairs).

(7) Conducts an ongoing education program for CIP personnel.

(8) Acts as the liaison and point of contact for official CIP communications with outside funding sources, including other Federal agencies and the Henry M. Jackson Foundation for the Advancement of Military Medicine.

c. Commanders of Naval MTFs

(1) Maintain responsibility for the CIP, the scientific integrity of research protocols, and protection of human and animal research subjects in their facility.

(2) Establish and support an institutional review system in one of the following formats, per references (c) and (d), if anticipating delegated local approval authority for clinical investigations:

(a) Institutional review board with all required aspects of review included.

(b) Institutional review board with subcommittees for scientific review and the protection of human subjects.

(c) Fully separate committees for scientific review and the protection of human subjects.

(3) Establish a radiation safety committee if using, or intending to use, radiation emitting equipment or agents in research.

(4) Establish a laboratory animal care and use committee if using, or intending to use, laboratory animals for research, per reference (e).

(5) Review the recommendations of the above committees, and approve or disapprove the research for conduct in their facility.

(6) Forward a complete protocol package to an MTF which has received delegated local approval authority for final approval, or forward an official copy of the locally approved protocol package to NSHS Bethesda within 30 days.

(7) Maintain and support staff and other infrastructure for the CIP proportionate to their delegated approval authority and the magnitude of their local program.

d. The CID Director

(1) Acts as the local program manager and central point of contact for individual investigators.

(2) Enforces higher authority policies.

(3) Promotes, manages, and supports the CIP within allocated resources.

(4) Prepares an annual CIP report for submission to NSHS Bethesda.

e. The Scientific Review Committee (SRC)

(1) Reviews all clinical investigation proposals for scientific adequacy, to include the following:

(a) Background, aims and hypothesis, and importance to Navy Medicine.

(b) Study design, specific and special procedures, time schedule to be followed, and the qualifications of the investigators.

(c) Population to be used.

(d) Precautions to minimize risks.

(e) Statistical analysis based on the number of subjects used and the study's design.

(2) Forwards written recommendations to the commander of the facility based on committee review and discussion.

f. Committee for the Protection of Human Subjects (CPHS)

(1) Reviews the recommendations of the SRC and radiation safety committee on the proposals within their areas of responsibility. In addition to responsibilities in reference (c), special emphasis should be given to the following:

(a) Ensures appropriateness of the subject populations to be used, particularly special populations, such as pediatric or active duty patients.

(b) Assesses risk-to-benefit ratio; for greater than minimal risk studies, assigns the medical monitor and the duties of the medical monitor.

(c) Reviews informed consent to ensure that there is no coercion to participate, subjects are legally and completely informed of all pertinent information, and all elements of informed consent required by references (c) and (d) are properly addressed.

(d) Reviews investigational drug clinical information brochure when using investigational drugs or biologics, and the manufacturers' brochure on those studies using investigational devices, per reference (f).

(e) Ensures subject privacy when storing identifiers and data.

(f) Monitors command responsibilities and liabilities regarding local sponsorship of investigational drugs or devices, per reference (f).

(2) Forwards all recommendations in writing to the commander of the facility. The commander has the authority to disapprove a committee's recommendation for approval; however, the commander may not order the committee to approve a protocol which the committee feels does not protect subjects' rights.

(3) Establishes guidelines for compliance on protocols under its responsibility.

(4) Reports promptly any cases of protocol noncompliance to the commander.

g. Institutional Review Board (IRB). An IRB can accomplish both scientific and human use reviews. This board, under the guidance of a chair appointed by the commander, performs combined functions of both the SRC and the CPHS, as defined above.

h. The IRB with Scientific Review and Protection of Human Subjects Subcommittees. Per reference (d), the separate subcommittees, guided by their respective chairs, report their recommendations to the IRB chair, who in turn reports to the commander.

i. The Radiation Safety Committee. This committee ensures that in the case of protocols involving the use of radiation emitting equipment or agents, all safety precautions for human subjects, animal subjects, and investigators are adequate and available.

j. Laboratory Animal Care and Use Committee (LACUC)

(1) Reviews all animal use protocols considering the following items and ensures all pertinent items are fully discussed within the proposal, per reference (e):

(a) Scientific rationale and the appropriateness of the animal species selected.

(b) Number of animals used, as well as the sex, weight, age, and source of the animals.

(c) Design of the experiment, procedure, or demonstration is adequate.

(d) Types of anesthesia, analgesic agents, and tranquilizers used are adequate to minimize pain or discomfort.

(e) Method of euthanasia employed.

(f) Potentially biohazardous agents.

(g) Adequacy of facilities, equipment, and trained personnel to conduct such research.

(2) Forwards a written summary of its recommendations to the commander of the facility for final action.

(3) Conducts semiannual inspections of the facility to review practices involving pain to animals and the conditions of animal care, and submits a written report to the commander of the facility, via the CID, after each inspection.

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Available at:

http://navymedicine.med.navy.mil/instructions/external/external.htm

What Is and Is Not A Clinical Investigation

1. Certain biomedical or health care system projects may use scientific methods, or involve the collection and/or statistical analysis of health data, but do not qualify as Navy CIP projects. They include, but are not limited to:

a. Activities that are designed to assess or improve the health care delivery system, such as:

(1) Surveys/questionnaires to staff or patients regarding opinions/preferences about the use of treatments, facilities, processes, practices, satisfaction or quality of care.

(2) Assessments of need for, or effectiveness of, staff educational programs.

(3) Cost effectiveness or process efficiency projects.

b. Case reports of clinical experiences and/or descriptions of new procedures/approaches.

c. Literature reviews.

d. Establishment of registries (populating databases) for unspecified uses in future studies that will require the preparation and submission of study-specific protocols.

e. Epidemiological surveillance or other epidemiological practices (versus epidemiological research) designed primarily to protect or enhance the health of broadly defined populations.

2. A project may not qualify for inclusion in the CIP but still may meet the definition of "research involving human subjects" and need to be reviewed consistent with 32 CFR 219 and prevailing Navy policies for protection of human subjects.

3. Regardless of whether or not the provisions of 32 CFR 219 pertain to projects excluded from the CIP, the technical approach of all projects should give appropriate consideration to the privacy of all individuals concerned, and to the confidentiality of their data.

CIP ACRONYMS

BUMED	Bureau of Medicine and Surgery
CID	Clinical Investigation Department
CIP	Clinical Investigation Program
CO	Commanding Officer
CPHS	Committee for the Protection of Human Subjects
DoD	Department of Defense
HIV	Human Immunodeficiency Virus
IRB	Institutional Review Board
LACUC	Laboratory Animal Care and Use Committee
MTF	Military Treatment Facility
NSHS	Naval School of Health Sciences
SRC	Scientific Review Committee